Computational Aspects of Molecular Science
USC, Los Angeles/Dr. Leonard Adleman

Objective

Construct the first automated molecular computer

- Ascertain the feasibility of the Sticker Model.
- Design and optimize methods and materials.
- Solve computational problems and build computational devices.

Approach

- Investigate two basic approaches for achieving low error rate separation
  - Attach DNA probes to solid support and capture target DNA by hybridization
  - Probes chemically bound to accessory molecules and placed in solution with target.
- Design and build a nucleic acid library for DNA computations
- Solve a 10 variable SAT problem manually
- Build a prototype DNA computer to solve a SAT problem using robotic technology

Schedule

Year One:

- Design, construction and testing of a nucleic acid library to perform a multivariable SAT calculation.
- Fabrication of solid supports containing attached DNA sequences.

Year Two:

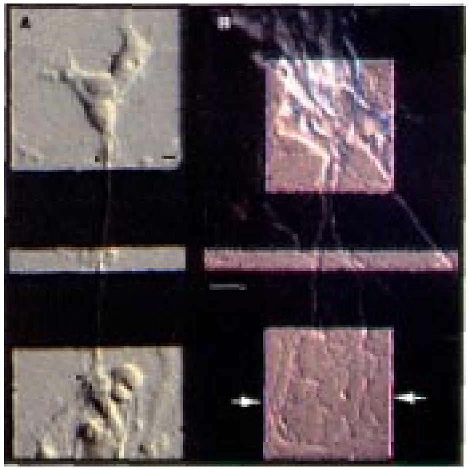
- Manual solution of a multivariable SAT problem.

Year Three:

- Construction of a robotically controlled DNA computer using commercially available components.

A Hybrid Neuron-Silicon Computational System for Pattern Recognition

University of Southern California/Theodore Berger



Objective

Develop a novel, hybrid neuron-silicon technology that will harness the computational capacity of cultured networks of hippocampal neurons for temporal and spatio-temporal pattern recognition applications.

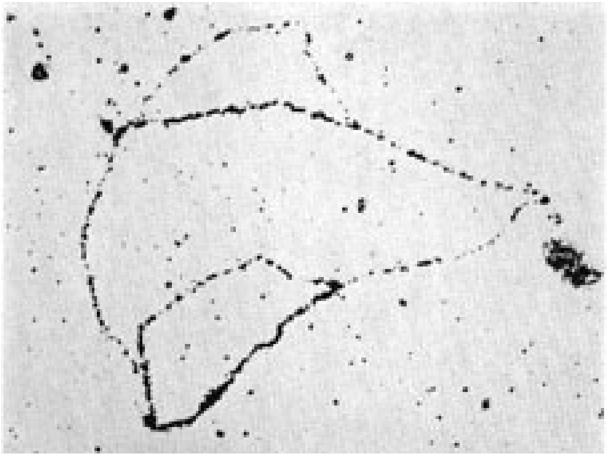
Approach

- Interface novel electrode arrays with hippocampal tissue slices & neuron cultures
- Develop growth techniques for cortical neurons on silicon substrates
- Develop neurobiologically-based pattern recognition systems
- Develop technologies to interface silicon-based computer systems and neurobiological systems
- Develop temporal dynamic hardware architecture

Schedule

- Silicon-based "conformal" multi-site electrodes for hippocampal slice cultures
- Unidirectional, convergence controlled-growth conditions for dissociated neuron cultures
- Hardware/software for optimizing tissue registration with the electrode arrays
- Signal processing paradigms for tissue-based feature extraction
- Analog VLSI implementation of dynamic synapse neural network for pattern recognition

Elemental Computation
The Molecular Sciences Institute/Dr. Sydney Brenner



Objective

Implement a new computational architecture for accurate simulation of biochemical processes involved in biosynthesis and regulation in biological systems.

Approach

- Develop software implementation of elementals that perform addition, sorting, and other basic computational functions.
- Implement software and dedicated silicon elemental based computing that perform nontrivial computations.
- Simulate prokaryotic regulatory pathway and eukaryotic signal transduction pathway.
- Demonstrate E.Coli cells that implement a nontrivial computation.

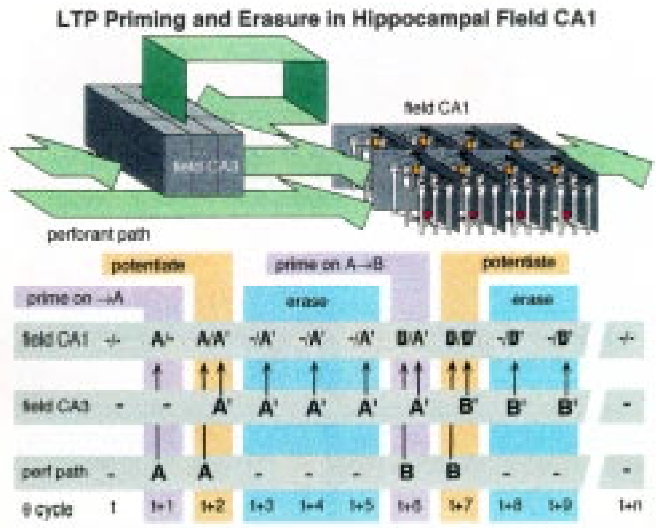
Schedule

Year One:
- Elementals that perform addition, sorting, and other basic computational functions.
- Elemental based software simulation of a synthetic metabolic pathway.

Year Two:
- Software and dedicated silicon implementations of elemental based computing that perform nontrivial computations.
- Elemental based software or hardware simulation of a prokaryotic regulatory pathway and a eukaryotic signal transduction pathway.

Year Three:
- Cell or plan for cell that implements a nontrivial computation.

Hybrid Computational Systems Based on Cultured Brain Slices
UC, Irvine/Richard Granger



Objective

Attempt to build a novel, brain-based computational device by connecting cultured hippocampal slices to an interface with 64 input/output lines.

Approach

- Connect “visual” input from simulated spatial environment to, and generate spatial cells within, a cultured hippocampal slice
- Analyze slice output for information contained in spatio-temporal patterns of cell activity
- Test interfaces that have greater numbers of input/output connections with cultured slices
- Compute with parallel slices
- Establish bi-directional communication between a cultured slice and an “observer”

Schedule

Year One:
- Develop background stimulation parameters imposing naturally occurring rhythms on cultured slices.

Year Two:
- Prepare a first prototype of the hybrid computational device.

Year Three:
- Establish two-way links between the cultured hippocampal slice and an ‘observer’ in the simulated spatial environment.

New Strategies & Architectures for Brain Imaging
Stanford University/ J. S. Harris

Objective

Develop new imaging techniques with the ability to resolve brain activity patterns at the individual neuron or individual synapse level while retaining the depth penetration powers and non-invasive characteristics of magnetic resonance imaging (MRI).

Approach

- Develop instrumentation optimized for both static & dynamic imaging of neural & tissues in embryos
- Develop molecules for labeling cells in a living embryo that are detectable by NMR imaging
- Perform multimodal imaging to establish the biological correlations between modes' features
- Compare genetic networks & advanced adaptive computing systems to determine their application to hybrid biological/electrical systems & computer architecture

Schedule

Year One:

- Adapt GFP and laser spectroscope systems for high resolution imaging.
- Develop micromachining and design instrumentation for high resolution NMR to image injected fly and fish embryos.

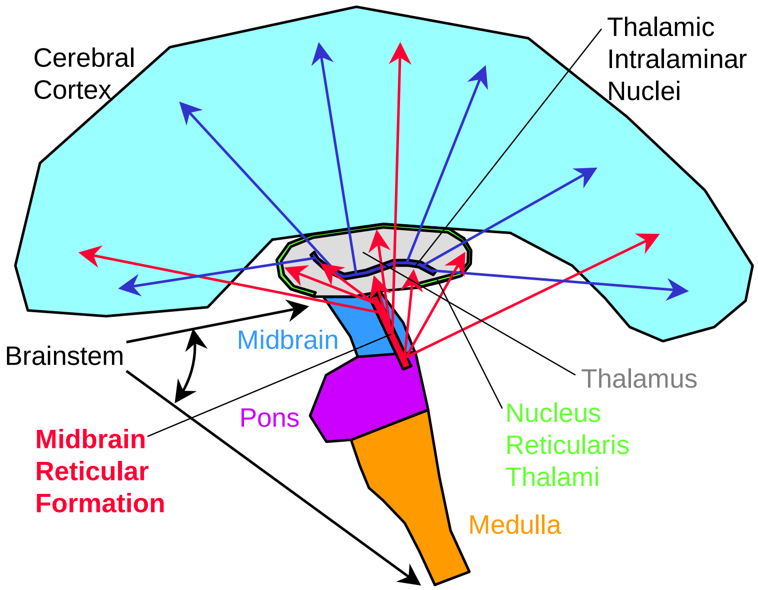
Year Two:

- Observe and analyze embryos expressing engineered transgenes coding for GFP.

Year Three:

- Construct fate maps of developing embryos using whole embryo NMR labels.

Neuromodem
HNC Software/Robert Hecht-Nielsen



Objective

Demonstration of a system that can learn to accurately recognize the representational codes expressed on a given cortical region of the brain and encode desired machine input to that region so that it will be correctly interpreted by the rest of the brain (given a reliable chronically implantable bioelectronic interface).

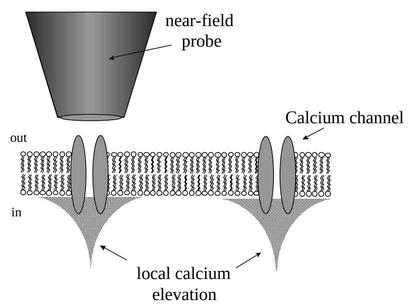
Approach

- Gather and enter the test and training data set
- Develop preprocessing modules
- Augment existing neural network software for implementation of *cortronic* architectures.
- Develop hierarchical representation for each type of input stream
- Build associator systems
- Develop image representation and expectation-driven object segmentation systems

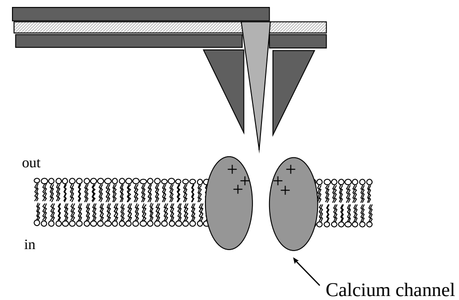
Schedule

- Year 1: Hierarchical Representations
  Processing Requirements
  Basic Time Sequence Associator
  Visual Object Invariant Features
- Year 2: Hierarchical Representations II
  Context-Aware Sequence Associator
  Visual Object Variant Features
- Year 3: Full-Scale Time Sequence Associator
  Expectation-Driven Object Segmentation

Nanoscale Field Localization for Manipulation and Probing of Computationally Interesting Biomolecules
University of Delaware/Daniel W. van der Weide



NSOM on ion channel



Microwave microscope on ion channel

Objective

Develop and apply new silicon tools for manipulating and probing neurons and ion channels. Employ tools in tandem with optical probes to understand structure, distribution and dynamics of ion channels.

Approach

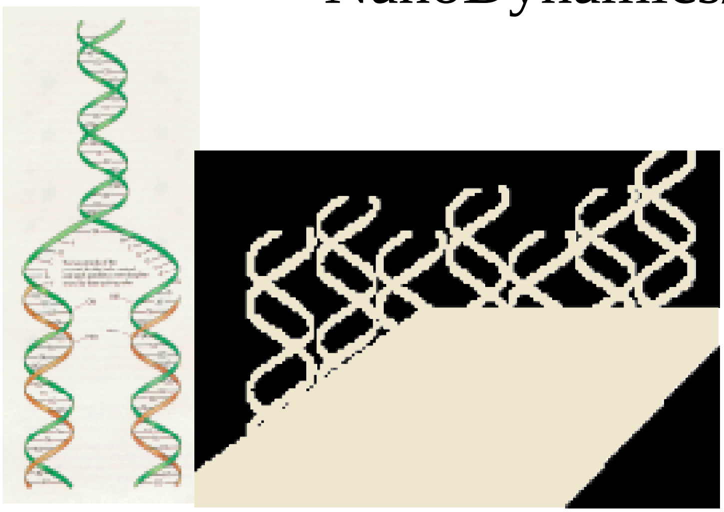
- Microfabricate multi-functional tips and transmission line cantilevers for use with external kHz-GHz signal generating and detecting equipment for neuronal membrane probes.
- Develop a multifunctional microwave microscope for biological science, and test its sensitivity and resolution.
- Use this biological “Nanoscilloscope” to study local ion fluxes at the level of individual ion channels without the need for fluorescent dyes.
- Determine the spatio-temporal dynamics of calcium channels in neurons.

Schedule

- Design and fabricate single tips and tip arrays.
- Use NSOM and near-field confocal optical microscopy (NCOS) to map distribution of functional ion channels.
- Image membranes with microwave microscope; develop high-frequency capacitive ion channel probe technique.
- Design and fabricate “microwave tweezers”.

A Hierarchical Key Structure for DNA Code Storage and Retrieval

NanoDynamics/Chia-Gee Wang



Objective

Develop screening techniques to allow efficient, logical design of DNA codes that will deliver a greatly improved “chip matrix” technology to molecular biology.

Approach

- Develop a generalized, *in vitro*, procedure for DNA cloning from any standard plasmid or lambda-based phage library.
- Demonstrate significant levels of an enzyme-mediated enrichment from cDNA libraries
- Integrate the enzyme-mediated enrichment with DNA-based chip matrix technology that will systematically locate tens of thousands of solid matrix bound single stranded probes homologous with the target DNA duplex.
- Automate the enzyme-mediated chip matrix.

Schedule

- Enzyme-mediated enrichment of a cDNA mini-library (4 months)
- Fidelity check on large scale three-some DNA inserts (10 months)
- DNA-Chip matrix mediated with enzyme, prototype demonstration (12 months)

Interfacing with Large-Scale Neuronal Ensembles
Massachusetts Institute of Technology/Matthew Wilson

Objective

Construct an interface which enables the delivery of synthetic inputs directly into sensory and memory systems of the brain and allows direct, remote access to the outputs of these systems in biological organisms performing high level information processing.

Approach

- Monitor neural patterns
  - Evaluate high-level neural signal processing in sensory, memory, and planning regions of the brain
- Neural Circuit Programming
  - Introduce synthetic sensory inputs into high-level neural systems with targeted computer stimulation
  - Integrate applied artificial neural signals with natural brain waves to allow training optimization
  - Use externally applied control signals to guide specific behaviors
  - Develop technique for remote task command & control

Schedule

1998 Setup and parameter configuration.

1999 Begin high-bandwidth telemetry design. Begin implementation of low-bandwidth telemetry system. Begin neural pattern control and navigation experiments.

2000 Low-bandwidth telemetry in place. Complete neural control experiments. Begin neural pattern recognition experiments.

2001 Full high-density interface with telemetry completed. All experiments completed.